

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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Serial No. 10/549,837	)	
	)	
Filed: March 16, 2004 (Int'l. Appl. No.	)	January 18, 2011
PCT/GB2004/001106)	)	
	)	
For: Method For The Production Of Metal	)	
Complexes	)	<u>/Andrew M. Lawrence/</u>
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Group Art Unit: 1625	)	Attorney for Applicant
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Examiner: John Mabry	)	
	)	
Confirmation No. 3759	)	

**PRE-APPEAL BRIEF REQUEST FOR REVIEW**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

The applicant hereby requests that a panel of examiners formally review the legal and factual bases of the rejections in the above-referenced application prior to the filing of an appeal brief. The applicant respectfully submits that the rejections should be withdrawn for the reasons concisely described herein.

Submitted herewith is a Notice of Appeal.

Claims 1-13 and 15-17 are pending, but claim 5 has been withdrawn as directed to a non-elected invention.

**CLAIM REJECTIONS — 35 U.S.C. §112, 2nd PARAGRAPH**

Claim 13 has been rejected as assertedly indefinite for reciting the term “metal complex”. In this respect, the examiner considers the term “metal complex” as being overly broad because “there are infinite numbers of possibilities of metal complexes.” *See* the official action dated July 16, 2010, at page 3. The applicant respectfully traverses the rejection.

A claim is considered definite as long as “the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent.” *See* M.P.E.P. §2173. Here, one of ordinary skill would readily understand the meaning of the term “metal complex” in view of the accompanying description and the teachings of the prior art as the term “metal complex” is a well

understood term of art in the chemical arts. Indeed, the statement at page 5 of the official action dated July 16, 2010, that “[i]n chemistry, a metal complex, is a structure consisting of a central atom or ion (usually metallic), bonded to a surrounding array of molecules or anions (ligands, complexing agents)” constitutes evidence regarding the understanding of one of ordinary skill in the art. Moreover, even assuming there are infinite numbers of possibilities of metal complexes, the recitation of the term metal complex in the preamble is largely irrelevant to the claim scope because *the steps positively recited in the body of the claim define the claim scope*.

In view of the foregoing, the indefiniteness rejection should be withdrawn.

**CLAIM REJECTIONS 35 U.S.C. §112, 1st PARAGRAPH**

All pending claims 1-13 and 15-17 have also been rejected as assertedly not enabled. Specifically, the examiner indicated that the claims are “not ... enabled for all aryl and heteroaryl compounds in complexes claimed and not ... enabled for forming complexes involving all “M” (metals as claimed). The applicant respectfully traverses the rejections.

The proper focus of the enablement inquiry is whether it would take undue experimentation for one of ordinary skill in the art to fully practice the scope of the invention. The applicants respectfully submit that the nature and quantity of experimentation necessary to practice the full scope of the invention is not undue or excessive. Any experimentation needed to practice the claimed invention is routine and within the scope of permissive experimentation as defined by *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), as explained in further detail below.

At page 8 of the outstanding action, the examiner acknowledged the disclosure as being enabling for M = iridium, but asserted that the disclosure is not enabling for M = rhodium, platinum, or palladium. The applicants respectfully disagree. Iridium and rhodium are well known to form halo-bridged dimers where  $n = 2$ . Platinum and palladium are well known to form halo-bridged dimers where  $n = 1$ . The literature and the cited art are replete with examples of the foregoing halo-bridged dimers, and the present application clearly demonstrates to one having ordinary skill how to form metal complexes, as claimed.

For example, the present application specifically exemplifies reacting iridium halo-bridged dimers as claimed. One of ordinary skill would immediately recognize that rhodium and iridium are isoelectronic species, and thus would have a reasonable expectation that these metals would behave similarly under similar reaction conditions, i.e., that these metals form the same kinds of coordination complexes when reacted as claimed. Consistent with this assertion, the Office is respectfully directed to the first and second paragraphs of Lamansky et al., *Inorg. Chem.*, 2001, 40:1704-1711 (2001), which was previously cited in this application and affirmatively demonstrates that these metals do in fact form the same kinds of metal complexes. This assertion can also be confirmed by referencing Tables 1-1 through 1-16 of EP 1349435 to Kamatani et al., which has also been cited in this application. Moreover, Lamansky et al., *Inorg. Chem.*, 2001, 40:1704-1711 (2001) explicitly discloses several octahedral iridium halo-bridged dimers with a number of different diaryl moieties  $Ar^1$ - $Ar^2$ . See *Id.* at Reaction Scheme 1 and Figure 1, for example. Based on the teachings in this document regarding

“isoelectronic Rh<sup>3+</sup> and Ir<sup>3+</sup> complexes” (*see* the first paragraph), rhodium would be expected to form similar halo-bridged dimers. In view of the foregoing, the applicants respectfully submit that the disclosure is enabling for M = rhodium.

Like rhodium and iridium, platinum and palladium are also well known to form halo-bridged metal dimers. *See*, for example, WO 02/15645 to Lamansky et al. at page 43, which explicitly references a synthetic strategy for forming platinum halo-bridged metal dimers, and pages 44-48, which discloses a number of different of number platinum halo-bridged metal dimers having different diaryl ligands. As platinum and palladium are isoelectronic, one of ordinary skill would have a reasonable expectation that these metals would behave similarly and form the same kinds of coordination complexes. Indeed, this expectation can be confirmed by reference to EP 1349435 to Kamatani et al. (*see*, for example, Table 1-17), which has also been cited in this application. In view of the foregoing, the applicants respectfully submit that the disclosure is enabling for M = platinum or palladium.

At page 8 of the outstanding action, the examiner acknowledged the disclosure as being enabling for “Ar<sup>1</sup>, Ar<sup>2</sup>, and L being pyridinyl and phenyl”, but not enabling “when Ar<sup>1</sup>, Ar<sup>2</sup>, and L are different.” The applicants respectfully disagree.

As an initial matter, the examiner’s indication that the terms aryl and heteroaryl are not well established terms of art is without a proper foundation. Indeed, the definitions provided at page 7 of the action are consistent with one another. The mere reference to “heterocyclic” in a definition does not mean that heteroaryl and heterocyclic mean the same thing. Rather, it is basic chemistry that a molecule must be cyclic in order to be aromatic. In view of the consistency between the various definitions provided by the examiner, the applicant again submits that these terms are well understood terms of art by those of ordinary skill in the art.

As explained above, numerous iridium, rhodium, platinum, and palladium complexes with a number of different diaryl ligands are specifically described, for example, in WO 02/15645 to Lamansky et al. and EP 1349435 to Kamatani et al., which were applied against the claims and are of record in this application. EP 1239526 to Tsuboyama et al., which was previously applied and overcome in this application, provides numerous additional examples of iridium, rhodium, platinum, and palladium complexes with a number of different diaryl ligands. Additionally, the application itself discloses a number of diaryl moieties Ar<sup>1</sup>-Ar<sup>2</sup>, and ligands, as claimed, at pages 11-12, and references WO 02/15645 to Lamansky et al., as disclosing other examples of suitable diaryl moieties Ar<sup>1</sup>-Ar<sup>2</sup>, and ligands, as claimed. Moreover, the diaryl moieties Ar<sup>1</sup>-Ar<sup>2</sup>, as claimed, *form at least one carbon-M bond by reaction of M with a carbanion of Ar<sup>1</sup>-Ar<sup>2</sup>*, and ligand L, as claimed, is a compound of formula Ar<sup>1</sup>-Ar<sup>2</sup> which *forms at least one carbon-M bond by reaction of M with a carbanion thereof*.

Finally, the examiner’s reliance on text from *In re Wiggins* as supporting the conclusion of non-enablement is an error in law that must be addressed.<sup>1</sup> *Wiggins* can be easily distinguished from the

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<sup>1</sup> The citation given at page 7 of the action (179 USPQ 421) and the excerpted text correspond to *In re Wiggins*, not *In re Hawkins* as indicated by the examiner.

presently claimed invention on the basis that the subject matter claimed in *Wiggins* relates to *compounds having anti-Parkinsonism activity*. The claimed subject matter claimed in *Wiggins* was determined to be so broad that it was entirely speculative as to the *required therapeutic activity*. No such concerns exist here where the presently claimed invention is directed to methods of forming metal complexes. *Wiggins* is therefore inapplicable to the subject matter at hand.

In view of the foregoing, the applicants respectfully submit that a large number of halo-bridged dimer complexes have been disclosed and/or are readily attainable in view of the prior art. Moreover, such complexes are known to form the metal complex end products recited in the pending claims. *The differences between the presently claimed invention and the cited art relate to the method in which the metal complexes are prepared.* In view of the foregoing analysis of documents cited (or previously cited) in this application and the extensive knowledge in the art itself, the applicant respectfully submits that the exemplified disclosure of the working examples may properly be extrapolated to other metals, diaryl moieties  $\text{Ar}^1\text{-Ar}^2$ , and ligands, in view of the general knowledge of one of ordinary skill in the art, as evidenced by the instant specification and (at least) the documents applied against the pending claims. Therefore, the applicants respectfully submit that the enablement rejections should be withdrawn.

#### **CLAIM REJECTIONS 35 U.S.C. §103(A)**

Claims 1-5 and 8-17 have been rejected as assertedly obvious over EP 1349435 to Kamatani et al. (hereafter “Kamatani”). Claims 1-13 and 15-17 have been rejected as assertedly obvious over WO 02/15645 A1 to Lamansky et al. (hereafter “Lamansky”).<sup>2</sup> The rejections are traversed.

None of the cited art discloses or even suggests forming a metal complex of formula  $\text{M}(\text{Ar}^1\text{Ar}^2)_n\text{L}$  by reacting a halo-bridged dimer complex according to formula (I) with a bidentate ligand L of formula  $\text{Ar}^1\text{-Ar}^2$  in the presence of an enabling ligand, as claimed. Rather, both Kamatani and Lamansky merely disclose reacting a halo-bridged dimer with a bidentate ligand such as acetylacetone (“acac”) or picolinic acid (“pic”) to break the stable chloro-bridged dimer and form monomeric complexes. Kamatani specifically teaches that the monomeric complex must then be *isolated and/or purified*, and *further reacted in a separate step* with a second bidentate ligand, which is capable of forming at least one carbon-to-metal bond with the metal of the complex to obtain a metal complex of formula  $\text{M}(\text{Ar}^1\text{Ar}^2)_n\text{L}$ , as claimed. *See*, for example, Kamatani at Example 28. Lamansky does not disclose further reaction of the monomeric complexes. *See* Lamansky at pages 41-47. Thus, the cited documents invariably involve two steps to form a metal complex, as claimed. Accordingly, these documents do not disclose forming a metal complex of formula  $\text{M}(\text{Ar}^1\text{Ar}^2)_n\text{L}$  by reacting a halo-bridged dimer complex according to formula (I) with a bidentate ligand L of formula  $\text{Ar}^1\text{-Ar}^2$  in the presence of an enabling ligand capable of breaking the halogen bridge of the complex according to formula I, as recited in claims 1-12 and 15-17.

Similarly, the applied documents also do not disclose forming a halo-bridged dimer and then reacting same with a reactive ligand capable of breaking the halogen bridge in a one pot process, as

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<sup>2</sup> The rejection of claim 14 is moot in view of its cancellation.

recited in claim 13. Rather, the art invariably discloses separating the intermediate halo-bridged dimer from the components of the mixture in which it is formed prior to reacting with any reactive ligand capable of breaking the halogen bridge.

The examiner relies on Dorwald as demonstrating that "it is well within the purview of the skilled artisan in the relevant art to reduce steps in order to achieve the desired product faster and in higher yields." See page 10 of the outstanding official action. In this respect, Dorwald discloses:

The synthesis of a structurally complex compound requires careful retrosynthetic analysis to identify the shortest synthetic strategies which are most likely to give rapid access to the target compound, ideally in high yield and purity. It is critical to keep the synthesis as short as possible, because, as discussed throughout this book, each reaction can cause unexpected problems, especially when working with structurally complex intermediates.

Dorwald contemplates redesigning a synthesis to have fewer steps. Admittedly, this goal is not new or revolutionary. Dorwald, however, does not disclose or suggest forming a metal complex of formula  $M(Ar^1Ar^2)_nL$  by reacting a halo-bridged dimer complex according to formula (I) with a bidentate ligand L of formula  $Ar^1-Ar^2$  in the presence of an enabling ligand capable of breaking the halogen bridge of the complex according to formula I, as recited in claim 1. Similarly, Dorwald also does not disclose or suggest forming a halo-bridged dimer and then reacting same with a reactive ligand capable of breaking the halogen bridge in a one pot process, as recited in claim 13. Thus, even if the Kamatani and Lamansky were modified in view of Dorwald, one would not arrive at the claimed invention.

The cited art invariably teaches *isolating and/or purifying, and further reacting an intermediate product in a separate step to obtain a metal complex as claimed*. While the examiner attempts to cast the claimed invention as "adjustment of particular conventional working conditions," the elimination of a step in a synthetic strategy is not routine optimization and was neither disclosed nor suggested by the teachings in the cited art. Indeed, the consistent teachings throughout the applied art to conduct two steps to obtain the claimed complexes is an indication that the methods, as claimed, are non-obvious.

### CONCLUSION

Allowance of all pending claims is respectfully requested.

Respectfully submitted,

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